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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GLAXO GROUP LIMITED Plaintiff, v. TEVA PHARMACEUTICALS USA, INC. and TEVA PHARMACEUTICAL INDUSTRIES LIMITED Defendants.	)	Civil Action No. 04-171-KAJ **CONFIDENTIAL** **FILED UNDER SEAL**

TEVA'S BRIEF IN OPPOSITION TO GLAXO'S MOTION FOR SUMMARY JUDGMENT DISMISSING TEVA'S AFFIRMATIVE DEFENSES AND CORRESPONDING COUNTERCLAIM ALLEGING INEQUITABLE CONDUCT DURING THE PROSECUTION OF U.S. PATENT NO. 5,068,249

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I. STATEMENT OF THE NATURE AND STAGE OF THE PROCEEDING

This lawsuit was filed after Defendant Teva Pharmaceuticals USA, Inc. ("Teva") filed an Abbreviated New Drug Application ("ANDA") for an oral ranitidine solution allegedly covered by U.S. Patent No. 5,068,249 ("the '249 patent"), which is owned by Plaintiff Glaxo Group Ltd. ("Glaxo"). The patent claims the use of ethanol to increase the stability of ranitidine in an oral solution. ('249 pat., col. 3, lines 1-4 (G000227-229)).[1] After the close of factual and expert discovery, both parties filed motions and supporting briefs for summary judgment of infringement/non-infringement and claim construction in accordance with the Court's Second Amended Scheduling Order of May 22, 2006. (D.I. No. 92). Glaxo also filed this motion, in which it seeks summary judgment and dismissal of Teva's affirmative defense and counterclaim that the '249 patent is unenforceable due to Glaxo's inequitable conduct before the U.S. Patent and Trademark Office ("Patent Office"). (D.I. No. 96). Teva files this brief in opposition to Glaxo's motion for summary judgment to dismiss Teva's affirmative defense and counterclaim.

II. SUMMARY OF THE ARGUMENT

Applicants for patents have a duty to prosecute patents in the Patent Office with candor and good faith, including a duty to disclose information known to be material to patentability. *Purdue Pharma L.P. v. Endo Pharm.*, Inc., 438 F.3d 1123, 1128-29 (Fed. Cir. 2006). This duty extends to every person involved in the prosecution of the patent. *See Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1178 n.6 (Fed. Cir. 1995) ("The duty to

[1] File history documents, referenced herein within the range G000111 through G000308, are attached as Exhibits 2 and 3 to the Joint Claim Construction Statement filed on June 30, 2006 (D.I. Nos. 106-107).

disclose information material to patentability rests on the inventor, on each attorney or agent who prepares or prosecutes an application and on every other individual who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, with the assignee, or with anyone to whom there is an obligation to assign the application.") A breach of this duty constitutes inequitable conduct. *Id.* at 1178. Inequitable conduct includes affirmative misrepresentations of a material fact, failures to disclose material information, or submissions of false material information. *Id.* An intent to deceive or mislead the Patent Office is also required to breach the duty. *Id.* Those charged with this duty must have complete candor, good faith and honesty with the Patent Office. *Id.* When there is doubt about the materiality of any information, that doubt should be resolved in favor of disclosure. *Brasseler, U.S.A. I., L.P. v. Stryker Sales Corp.*, 267 F.3d 1370, 1380 (Fed. Cir. 2001) (citing *Critikon, Inc. v. Becton Dickinson Vascular Access*, 120 F.3d 1253, 1257 (Fed. Cir. 1997)).

During its prosecution of the '249 patent application, Glaxo failed to disclose at least two pieces of material information to the Patent Office. First, Glaxo's Dr. Hempenstall did not submit all of the data it had on the stability of ranitidine in the presence of ethanol. Hempenstall's intentional submission of incomplete data was what convinced the Examiner to allow the patent. Some of the withheld data showed that ethanol did not improve the stability of ranitidine to a statistically significant degree. This was directly contrary to what was being argued to the Examiner. Second, the inventor, Dr. Long, did not disclose a related, Tagamet® formulation containing ethanol. Glaxo was aware of this formulation, and it was much more material than the references cited to or by the Examiner. In fact, it was the only prior art that showed an H2 blocker

in an oral solution with ethanol that was commercially available and therefore, presumably stable. These two omissions served to limit the Examiner's evaluation of the '249 patent application and, together with other evidence in this case, create a strong inference that Glaxo intended to deceive the Patent Office.

At the very least, there are factual issues in dispute, and this Court should determine at trial whether Glaxo's omission of information was material and intentional, constituting inequitable conduct that renders the '249 patent unenforceable. Moreover, Glaxo offers no compelling reason why this Court should adopt the legal conclusions of the court in the *Pharmadyne*[2] case and deprive Teva of its constitutional right to a trial on the different parties, facts and evidence presented in this case.

III. STATEMENT OF THE FACTS

A. Introduction

Glaxo alleges that Teva's proposed, generic ranitidine oral syrup formulation infringes Glaxo's '249 patent under the doctrine of equivalents. The '249 patent is entitled "AQUEOUS RANITIDINE COMPOSITIONS STABILIZED WITH ETHANOL." The critical difference between the patented composition and Teva's proposed formulation is that Teva's formulation uses while the patented formulation uses ethanol.[3]

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The cornerstone of Glaxo's patent is the limitation – "a stabilizing effective amount of ethanol." (Col. 3, line 3). That patentable distinction was not easily obtained, however, and incorporates Glaxo and the Examiner's understanding that such an amount

[2] 32 F. Supp. 2d 265 (D. Md. 1998).

[3] Teva also uses different amounts of most of the other excipients and versus 10 % (Glaxo). (D.I. No. 105, Exhibit 1 to Teva's Opening Brief in Support of Motion For Summary Judgment of Non-Infringement at A004, Anderson Report, March 16, 2006, ¶ 52) (emphasis added).

of ethanol must necessarily be "demonstrated . . . by . . .experimental data to show a definite improvement over the [prior art]." (G000200). The Examiner repeatedly and consistently rejected the application as an obvious variant over the prior art. To overcome the rejections, Glaxo ultimately was forced to submit a declaration attesting to ethanol's "surprising" and "significant" ability to enhance "the stability of ranitidine." (G000209, ¶ 5). That declaration, however, was misleading and incomplete; it contained cherry-picked data that served to support Glaxo's claims of substantially enhanced ranitidine stability with ethanol while excluding data to the contrary.

B. The Prosecution History

Glaxo began prosecuting the '249 patent on December 11, 1987, as Application No. 07/131,442 ("the '442 application"). (G000237-238). After it filed the '442 application with the Patent Office, but prior to the first examination on the merits, Glaxo submitted an "Information Disclosure Statement" with "the following information, which may be considered material to the prosecution of the ['442] application:" (1) U.S. Pat. No. 4,128,658,[4] (2) U.S. Pat. No. 4,585,790,[5] and (3) a publication by one of its scientists, John Padfield, titled, "The Chemical Use of Ranitidine." (G000258-261).[6]

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[4] The '658 patent, entitled "AMINOALKYL FURAN DERIVATIVES," is equivalent to "British Patent Specification No. 1,565,966," which is disclosed in the specification. The '966 patent makes a passing reference to "an oral syrup" of ranitidine, but otherwise does not teach or claim its manufacture. (G000258, G000254, lines 4-10).

[5] The '790 patent, entitled "PHARMACEUTICAL COMPOSITIONS," teaches an aqueous formulation of ranitidine with "enhanced shelf life" at "a pH in the range 6.5-7.5." ('249 patent (Abstract)). It is the U.S. equivalent of U.K. patent GB 2,142,820 to Padfield ("the '820 patent").

[6] An Information Disclosure Statement ("IDS") is used by patent applicants, and individuals associated with the patent application, to fulfill their "duty to disclose information material to patentability" pursuant to 37 CFR § 1.56. The mere filing of an IDS, however, does not automatically mean that the duty has been met. *See Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, 326 F.3d 1226, 1242 (Fed. Cir. 2003) (inequitable conduct and unenforceability found upon untimely submission of material prior art).

The Examiner, however, never considered this prior art during the prosecution of the '442 application. Instead, he rejected the pending claims of the application for obviousness based on two *Chemical Abstracts* references, which the Examiner had found on his own and entered into the file history.[7]

The Examiner's first Office Action on the '442 application rejected all of the claims of the application because the *Chemical Abstracts* taught, "the conjoining of ranitidine and an alcohol, e.g. ethanol." (G000265). In response, Glaxo argued, "the art does not teach the cojoining of ranitidine and ethanol in a pharmaceutical composition." (G000268) (emphasis added).

Glaxo argued that *Chemical Abstracts* 97: 61014g (1982) "relates to the Glaxo patent for a new polymorphic form of ranitidine hydrochloride (designated form 2) and includes a description of processes for its production." (G000269).

Glaxo argued that *Chemical Abstracts* 104: 102280z (1986) "relates to a paper in a Scandinavian journal indicating the presence of ethanol in a person's diet did not adversely affect the gastric acid secretion inhibiting properties of ranitidine." (*Id.*)

On the second Office Action, the Examiner maintained his rejections to all claims "over Chemical Abstract (both) under 35 USC 103" for the same reasons stated in the first Office Action. (G000272). The Examiner made his second rejection final. *Id.* In lieu of responding, Glaxo abandoned the '442 application on July 3, 1989. (G000275).

Glaxo filed its second application on April 28, 1989, as Application No. 07/344,620 ("the '620 application"). On his own accord, the Examiner entered into the record of the '620 application the *Chemical Abstracts* references that he had found during

[7] *Chemical Abstracts* is a publication of Chemical Abstracts Service, which is a division of the American Chemical Society. *Chemical Abstracts* contains abstracts of patents and articles published in major scientific journals.

the examination of the '442 application. (G000133). Glaxo did not resubmit the '658 and '790 patents or the Padfield article as "material" prior art. Instead, Glaxo submitted U.K. Patent Application 2,120,938A, entitled "ANTI-ULCER PHARMACEUTICAL COMPOSITIONS CONTAINING SALICYLIC ACID OR ITS SALTS." The '938 application teaches the experimental use of ranitidine or cimetidine[8] in the treatment of ethanol-induced gastric lesions in rats. (G000147, G000150, lines 52-57) (emphasis added).

On the first Office Action of the '620 application, the Examiner rejected all of the claims as obvious in view of *Chemical Abstracts* ("the art teaches the cojoined use or use [sic] of ranitidine and an alcohol (ethanol)"). (G000132). Glaxo argued in response, "the art does not teach the cojoining of ranitidine and an alcohol in a pharmaceutical composition which is an aqueous formulation for oral administration." (G000141) (emphasis added). Glaxo further argued that *Chemical Abstracts* did not teach that "ethanol" could "enhance . . . the stability of ranitidine." (G000142).

The Examiner was not persuaded and again rejected all of the claims of the '620 application as obvious over the *Chemical Abstracts* references. The Examiner stated that, "[a]s for the allegation of enhanced stability, it has not been demonstrated for the compositions urged as contrasted with any of other pH parameters."[9] (G000161). The Examiner made this rejection final.

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[8] Cimetidine is Tagamet®. *Pharmadyne* at 301.

[9] Although the basis for the Examiner's comment is unclear, the Examiner might have been referring to the pH parameters listed in the application or the '820 Padfield patent (or its U.S. equivalent, the '790 patent). (G000191, lines 57-60; G000285 (Abstract)). Glaxo had already received a patent on the use of pH to stabilize ranitidine, and this information had been disclosed to the Examiner, but not considered, in the previous '442 application. (G000258-261).

In response to the final rejection of all claims of the '620 application, Glaxo filed a "Request for Filing File Wrapper Continuation Application Under 37 C.F.R. 1.62" on March 14, 1990. This allowed Glaxo to continue prosecuting the application under a new Application number, 07/494,804 ("the '804 application"). On May 4, 1990, the Examiner again rejected "all" of the claims of the application as obvious in view of the same *Chemical Abstracts*. (G000141).

Glaxo responded to the May 1990 Office Action with the same arguments as before. Namely, that *Chemical Abstracts* did not teach the enhanced stability of ranitidine in an aqueous oral formulation by the addition of ethanol. (G000175-176). Glaxo represented that it would submit "a Declaration to substantiate the unexpected effect of ethanol in enhancing the stability of ranitidine in aqueous oral formulations." (G000177) (emphasis added). Glaxo also submitted patent GB 2,142,820A and its French equivalent, Pub. No. 2,547,727. (G000177, ¶ 3).

The '820 patent, entitled "AQUEOUS COMPOSITIONS OF RANITIDINE," and its French equivalent, "PHARMACEUTICAL COMPOSITIONS," teach aqueous-based oral formulations containing ranitidine that have enhanced shelf life within a narrow pH range of 6.5-7.5. (G000192, lines 19-21; 58-59). Glaxo also mentioned "French application 2,501,206" in its response. (G000177, ¶ 4). Glaxo stated that the '206 application discloses "pharmaceutical formulations" of "novel compounds which are structurally different than ranitidine." (*Id.*) Glaxo, however, did not submit the '206 application to the Patent Office.

The only prior art before the Examiner during the prosecution of the '249 patent related to the experimental synthesis of ranitidine using ethanol (*Chemical Abstracts* 97:

61014g), the experimental effect of ethanol on ranitidine's ability to inhibit gastric acid secretion in humans (*Chemical Abstracts* 104: 102280z), the effect of ranitidine or cimetidine on ethanol induced lesions in rats (the '938 application), and pharmaceutical compositions of ranitidine (or cimetidine) without ethanol (the '820 patent and the '938 application).

On January 22, 1991, before Glaxo submitted any declaration to the Patent Office, the Examiner issued its second Office Action on the '804 application. The Examiner stated that Glaxo had overcome the objections made in the May 4, 1990, Office Action "by the amendment filed on 10/31/90," but he still rejected all claims as obvious in view of the '820 patent. The '820 patent teaches ranitidine formulations having enhanced stability at pH 6.5 to 7.5, the same pH range claimed in the '249 patent. (G000199-200). In support of this new rejection, the Examiner stated, "[i]t has not been demonstrated in the record, by means of experimental data, that the applicant's invention produces any unexpected results." (G000200). The Examiner also stated that, "[a]bsent evidence to the contrary, the addition of ethanol is considered merely to be a choice among known conventional excipients." (*Id.*)

In direct response to the Examiner's request for data, Glaxo submitted a declaration of one of its scientists, Dr. Hempenstall, containing experimental data. Dr. Hempenstall was a Research Leader at Glaxo at the time and is not an inventor of the '249 patent. (G000208, ¶ 1). Dr. Hempenstall's declaration purported to show "a significant and surprising enhancement in the stability of the ranitidine . . . by the addition of ethanol to the formulation." (G000209). To show "a highly significant and valuable improvement" in the "the acceptable shelf life for an aqueous formulation

containing ranitidine hydrochloride," Dr. Hempenstall compared a formulation with 0% ethanol to one with 7.5% ethanol. (G000210-211). Dr. Hempenstall defined "acceptable shelf life" as "the time (in months) for 5% ranitidine loss calculated as the lower 95% confidence limit." (G000210). However, the information that Dr. Hempenstall submitted was incomplete.

C. The Withheld Information

Dr. Hempenstall knowingly submitted incomplete data to the Patent Office in order to convince it to allow the '249 patent. The *Pharmadyne* court expressly found that Dr. Hempenstall 'excluded unfavorable data.' *Pharmadyne* at 313. This, alone, creates a strong inference that Dr. Hempenstall intended to deceive the Patent Office. Redacted

The inference is further reinforced by the fact that another Glaxo employee, Dr. Bird, wrote a memo in which she analyzed and concluded that the effect of ethanol on the stability of ranitidine was (D.I. No. 105, Exhibit 12 at A054, G000919). Dr. Hempenstall read Dr. Bird's memo (Exhibit A at B002, Hempenstall Depo., pp. 205-206).[10] Nonetheless, Dr. Hempenstall hid this information from the Patent Office and argued with incomplete data that there was a "highly significant" improvement in ranitidine stability using ethanol. (G000211).

There also is evidence that Dr. David Long, the sole inventor of the '249 patent, intentionally withheld a prior art Tagamet®/ethanol solution from the Patent Office. The Tagamet®/ethanol solution was the only piece of prior art in which a commercial H2

[10] By stipulation of the parties and this Court's Order of May 12, 2006, the deposition testimony of Glaxo witnesses Dr. David Long, Dr. John Hempenstall, Dr. John Padfield, Dr. Ian Winterborn, Gillian Amphlett and Nadeem Elahi in the *Glaxo v. Pharmadyne* case are admissible evidence in this case. (D.I. No. 87).

blocker, such as ranitidine, was combined with ethanol in an oral solution that was commercially available and, therefore, presumably stable. No art cited by Glaxo or the Patent Office contained all of these attributes. Dr. Long admitted in his deposition in the *Pharmadyne* case that he knew of the Tagamet®/ethanol solution before the first application for the '249 patent was filed.[11]

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(Exhibit B at B004, Long Depo. p. 53, lines 14-17). Neither Glaxo nor Dr. Long ever submitted this piece of prior art to the Patent Office. Yet, none of the considered prior art taught a commercial H2 blocker in a stable pharmaceutical composition containing ethanol.

The "unfavorable data" that Hempenstall "excluded" and the Tagamet®/ethanol solution were highly material and not cumulative of any art before the Examiner. The evidence, and inferences from the evidence, show that Glaxo intentionally withheld: (1) all of the data regarding ethanol's effect on the stability of ranitidine, and (2) the Tagamet®/ethanol solution. Genuine issues of material fact remain, that warrant denial of Glaxo's motion to dismiss Teva's inequitable conduct defense and counterclaim.

[11] The '249 patent was first filed in the United Kingdom on December 12, 1986. ('249 patent, cover).

IV. ARGUMENT

A. The *Glaxo v. Pharmadyne* Opinion Does Not And Should Not Preclude Teva From Presenting Its Own Evidence Of Glaxo's Inequitable Conduct.

The public policy underlying the principles of preclusion, whereby potentially meritorious defenses may be barred from judicial scrutiny, has led courts to hold that the circumstances for preclusion "must be certain to every intent." *Russell v. Place*, 94 U.S. 606, 610 (1876) (denying preclusion of an invalidity defense in a patent infringement case based on plaintiff's prior successful infringement action against another party); *see also Sharp Kabushiki Kaisha v. Thinksharp, Inc.*, 448 F.3d 1368, 1372 (Fed. Cir. 2006) ("When a party did not have an opportunity to litigate disputed issues, a decision to permit such litigation is favored.")

These cases stand for the proposition that unless absolute identity of issues and parties exist, issues and evidence decided in one case should not be imputed to a litigant in a different case. As succinctly stated by the Supreme Court in *Blonder-Tongue Lab. v. University of Illinois Found.*, 402 U.S. 313, 329-30 (1971):

> [T]hose who never appeared in a prior action . . . may not be collaterally estopped without litigating the issue. They have never had a chance to present their evidence and arguments on the claim. Due process prohibits estopping them despite one or more existing adjudications of the identical issue which stand squarely against their position.

(internal citations omitted).

Accordingly, the court's findings and conclusions in the *Pharmadyne* case should not preclude Teva from making its own arguments and presenting its own evidence on the materiality and intent of Glaxo's omissions to the Patent Office, even if the arguments and evidence are essentially the same.

The *Pharmadyne* decision is not binding precedent by this Court or any Court of Appeals. In addition, the *Pharmadyne* court's legal conclusions on inequitable conduct were premised on different evidence. For example, one of Glaxo's expert witnesses in *Pharmadyne*, Dr. Wray, is now deceased according to Glaxo. He testified about the chemical and clinical differences between cimetidine ("Tagamet®") and ranitidine. *Pharmadyne* at 301. In reliance on his testimony, the *Pharmadyne* court concluded that Pharmadyne had failed to prove that the Tagamet® formula in ethanol was material prior art to the '249 patent. *Pharmadyne* at 310.

Glaxo and Teva did not stipulate to the admissibility of Dr. Wray's trial or deposition testimony. Glaxo's expert, Dr. Anderson, has not opined on the materiality of the Tagamet® prior art. Given the different evidence in this case relating to the materiality of the Tagamet® reference, *Pharmadyne* has no bearing on how this Court decides to weigh these admissible facts at trial.

B. The Standard For Inequitable Conduct In This Case Is Whether The Examiner Would Have Considered The Information Glaxo Omitted Important.

Because the patent application that led to the issuance of the '249 patent was filed prior to 1992, information is deemed material if there is a "substantial likelihood that a reasonable examiner would have considered it important in deciding whether to allow the application to issue as a patent." *Warner-Lambert Co. v. Teva Pharmaceuticals USA*, 289 F. Supp. 2d 515, 534 (D.N.J. 2003) (citing 37 C.F.R. § 1.56(a) (1987); *Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1179 n.8 (Fed. Cir. 1995). "Materiality is determined from the viewpoint of a reasonable patent examiner, and not the subjective beliefs of the patentee." *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, 326 F.3d 1226, 1238 (Fed. Cir. 2003). "Materiality and intent are factual issues." *J.P. Stevens & Co. v. Lex*

Tex, Ltd., 747 F.2d 1553, 1562 (Fed. Cir. 1984). A false affidavit, standing alone, is sufficient to render a patent unenforceable. *Digital Control, Inc. v. Charles Mach. Works*, 437 F.3d 1309, 1321 (Fed. Cir. 2006). Moreover, in the summary judgment context, all inferences must be made in favor of the non-movant. *Digital Control, Inc.*, 437 F.3d at 1316. Under these standards, there is enough evidence of materiality and intent to deceive to deny Glaxo's motion.

C. Triable Issues Of Fact Exist On Materiality And Intent To Deceive By Glaxo's Failure To Submit All Of Its Stability Data.

After repeatedly failing to convince the Examiner that ethanol, as compared to other "known conventional excipients," had the unique ability to significantly enhance the stability of ranitidine, Glaxo finally submitted data in the Declaration of Dr. Hempenstall on May 10, 1991, as part of a Request for Reconsideration of the rejections made in January 1991. (G000204, G000208-211). The Patent Office relied on this data, found it persuasive, and allowed the patent. (G000212).

As it turns out, Dr. Hempenstall did not submit all of Glaxo's stability data to the Patent Office. The *Pharmadyne* court found that Hempenstall "excluded ... unfavorable data." *Pharmadyne* at 313. Dr. Hempenstall's failure to submit all of Glaxo's stability data, including data that was unfavorable to its claim of enhanced ranitidine stability, led the *Pharmadyne* court to find "improper behavior by Glaxo in prosecuting the ['249] patent." *Pharmadyne* at 312.[12] The *Pharmadyne* court was "troubled by Glaxo's failure to present all of the statistical data to the PTO." *Id.*

Glaxo's reliance on the *Pharmadyne* case is curious because it is fatal to its summary judgment motion. The *Pharmadyne* court clearly found that all of Glaxo's experimental data was material, but not disclosed. "There is no question that Glaxo should have provided the Patent Office with all the experimental data from both the

[12] Although *Pharmadyne* does not preclude Teva from presenting its case, the finding is instructive. It shows an inference that can be drawn from the evidence presented in that case. By stipulation in this case, most of the trial testimony and exhibits that were before the court in *Pharmadyne* are admissible before this Court. (Order of May 12, 2006, D.I. No. 87). This Court will have to examine the evidence and testimony from the *Pharmadyne* case to arrive at its own conclusions on inequitable conduct. Interestingly, the *Pharmadyne* case was not dismissed on summary judgment. There were real, triable issues and facts to support them. That same evidence is before this Court and, as in *Pharmadyne*, creates factual triable issues this Court should determine after viewing all of the evidence.

United Kingdom and United States studies." *Id.* It also led the court to conclude that there was intent; "the appearance of improper behavior by Glaxo in prosecuting the patent, therefore, appears great." *Id.* Based on these findings alone, there is a factual issue regarding the materiality of the withheld data and the intent to withhold it.

Intent also can be inferred from other evidence in the case, and this creates a factual issue that precludes summary judgment. Dr. Hempenstall's intent to deceive the Examiner can be inferred from his failure to tell the Examiner about a report by Dr. Bird, another Glaxo scientist.

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Dr. Bird's report was prepared for the express purpose of being used

(Exhibit 12 to at A054 (G000919)) (D.I. No. 105). Dr. Bird analyzed the stability data using (*Id.*); *see Pharmadyne* at 311. As stated in the Bird memo,

(*Id.*) (emphasis added). After analyzing all of the data, however, Dr. Bird

(*Id.*) (emphasis added). She further wrote:

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(*Id.*) (emphasis added) (Exhibit A at B002, Hempenstall Depo. pp. 205-206). Despite knowing Dr. Bird's , Dr. Hempenstall submitted a declaration to the Patent Office that omitted " " from the and selected only some of the data. With this cherry-picked data, Dr.

Hempenstall argued to the Patent Office that there was a "highly significant and valuable improvement." (G000211) (emphasis added). Dr. Hempenstall did not tell the Patent Office that Dr. Bird's analysis of ' showed an effect that was " ," and he did not tell the Patent Office that his conclusions of "highly significant" results were from only a subset of Glaxo's " ."[13] Certainly, these facts create an inference that Dr. Hempenstall intended to deceive the Patent Office when he presented incomplete data and characterized those results as "highly significant."

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The evidence presented in the *Pharmadyne* case created triable issues of materiality and intent with respect to the data Dr. Hempenstall supplied to the Patent

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[13] Glaxo has again used incomplete data in this case to show that Teva's formulation infringes the '249 patent. Dr. Anderson, Glaxo's expert,

(Exhibit C at B006-B007, Anderson Depo. at pp. 149-150, ll. 4-25, 1-10). He only analyzed specific Glaxo " " (Exhibit C at B007, Anderson Depo. at p. 150, l. 10). At his deposition, he was shown additional stability data that he had not used in his calculations:

(Exhibit C at B006, Anderson Depo. p. 149, ll. 9-22)

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(Exhibit C at B008-B009, Anderson Depo. pp. 156-157, ll. 13-25, 2-4). Thus, it appears that Glaxo's practice of selectively highlighting subsets of data that aligns with its arguments continues even today.

Office. Faced with this evidence, the *Pharmadyne* court found the withheld data to be material. The *Pharmadyne* court also concluded that Dr. Hempenstall did not have an intent to deceive, but this Court is not bound by that finding. After reviewing the evidence, this Court may or may not agree with the *Pharmadyne* court, but it is improper to reach that conclusion on a summary judgment motion.

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Dr. Bird's memo provides a strong inference that Dr. Hempenstall knew what he was doing when he left out the U.K. data and argued that the incomplete data showed "highly significant" results. (G000211) Dr. Bird had

, but did not disclose its contents or conclusions to the Examiner. As a direct result of Dr. Hempenstall showing a "highly significant and valuable improvement," Glaxo received its '249 patent. (G000211-212). These are strong, triable issues of fact and Glaxo's motion should be denied.

E. Triable Issues Of Fact Exist On Materiality And Intent To Deceive By Glaxo's Failure To Submit The Tagamet®/Ethanol Prior Art.

During the prosecution of the '249 patent, the Patent Examiner rejected the patent claims based on a number of references. One was *Chemical Abstracts* 97: 61014g (1982), which taught ethanol as a solvent in the synthesis of ranitidine. (G000134). Another was *Chemical Abstracts* 104: 102280z (1986), which taught the effect of ranitidine on meal-induced gastric pepsin and acid secretion and the influence of adding ethanol to the meal. (G000135). The Examiner also rejected the application on the Padfield '820 patent, which taught ranitidine in oral solution stabilized by pH. (GB 2,142,820 and its equivalent FR 2,547,727 (G000182-195)). Other prior art disclosed

tests in which ethanol was used to induce stomach lesions in rats, and then the effect of ranitidine on the lesions was tested. (GB 2,120,938 (G000147-159)).

The Examiner had no reference containing a stable, commercial H2 blocker in an oral solution with ethanol. Had the Examiner had such a reference, his rejections would have been much stronger. Indeed, such a reference would not have been cumulative of the references cited in the application, and it would have been more material than the references cited in the patent application. The Tagamet®/ethanol solution was such a reference, and it was not disclosed to the Patent Office.

The prior art contained a solution of Tagamet® and ethanol. Tagamet® is cimetidine, an H2 blocker like ranitidine. Consistent with Dr. Long's testimony that he was aware of the Tagamet® product with ethanol in 1985, the 1985 Physician's Desk Reference ("PDR") lists Tagamet® Liquid as follows:

> Each 5 ml. (1 teaspoonful) contains, in aqueous solution, cimetidine hydrochloride equivalent to cimetidine, 300 mg.; alcohol, 2.8%.

(Exhibit D at B011, 1985 PDR, p. 1974) (emphasis added).

The 1988 PDR provided a more complete formula and disclosed:

> Each 5 ml. (one teaspoonful) of clear, light orange, mint-peach flavored liquid contains cimetidine hydrochloride equivalent to cimetidine, 300 mg.; alcohol, 2.8%. Inactive ingredients consist of FD&C Yellow No. 6, flavors, methylparaben, polyoxyethylene polyoxypropylene glycol, propylene glycol, proplyparaben, saccharin sodium, sodium chloride, sodium phosphate, sorbitol and water.

(Exhibit E at B014, 1988 PDR, p. 2031) (emphasis added).

As show above, the Tagamet®/ethanol product contained all of the ingredients of Glaxo's patented formula except for ranitidine and methylcellulose.[14] The Redacted Tagamet®/ethanol formula also contained , which is what Teva uses.

The *Pharmadyne* court's conclusion that "the Tagamet reference was cumulative and not material" was wrong. *Pharmadyne* at 310-311. No prior art before the Examiner so closely matched the product described in the '249 patent application as the Tagamet®/ethanol reference. The *Chemical Abstracts* only disclosed ethanol in the synthesis of ranitidine and experimental use in humans, not in solution with ranitidine. The ethanol in this reference was not in the final ranitidine product; it was removed. Glaxo's '938 patent described the use of ethanol to induce lesions. The '820 patent disclosed a ranitidine formulation without ethanol. No prior art before the Examiner showed an H2 blocker combined with ethanol in a presumably stable commercial product.

Dr. Long, the inventor of the '249 patent, was aware of the Tagamet®/ethanol solution but did not disclose it to the Patent Office. *Pharmadyne* at 278; (Exhibit B at B004, Long Depo. p. 53, lines 14-17). This Court, therefore, should analyze for itself the materiality of the Tagamet®/ethanol disclosure and Dr. Long's intent to deceive the Patent Office.

Certainly, there is a triable issue about whether the Tagamet®/ethanol solution was material. It had features important to the invention unlike any other piece of prior art. It combined an H2 blocker in an oral solution with ethanol in a presumably stable

[14] The "illustrative" example shown in the '249 patent discloses ranitidine, ethanol, phosphate buffers, methylcellulose, paraben preservatives, sorbitol, flavor and water. (Col. 2, ll. 47-64) (emphasis added).

commercial product. No other reference was this close to the invention. The Tagamet®/ethanol solution, therefore, was material and non-cumulative.

As to intent, there is sufficient information to infer intent. Dr. Long was aware of the Tagamet®/ethanol solution. (*Id.*) It would be incredible that he would not realize that the Tagamet®/ethanol solution was a better reference than anything the Patent Office had found or cited. This, alone, or coupled with Dr. Hempenstall's conduct, which could infer a corporate culture of non-disclosure, certainly results in a triable issue on intent. After all, the Federal Circuit has said that "smoking guns" are rarely found evidencing intent, nor is a smoking gun required. *See Warner-Lambert Co. v. Teva Pharms. USA, Inc.*, 418 F.3d 1326, 1346 (Fed. Cir. 2005) (Smoking gun evidence is not required in order to find intent to deceive.) Although there is no smoking gun showing that Dr. Long intentionally withheld the Tagamet®/ethanol solution from the Patent Office, the facts could lead to that conclusion and, therefore, preclude a grant of summary judgment.

Glaxo's brief spends its time arguing why the Tagamet®/ethanol solution is different from the invention. These distinctions and arguments miss the point. The Tagamet®/ethanol solution was more material than any other reference disclosed to the Patent Office or cited by the Patent Office. Glaxo, in meeting its obligation of "complete candor" should have disclosed this solution to the Examiner, told him of the similarities to the invention and then argued the differences that are now found in its brief. *See Rohm & Haas Co. v. Brotech Corp.*, 127 F.3d 1089, 1093 (Fed. Cir. 1997). That would have been "complete candor." *Id.* Glaxo did not do this, and its after-the-fact denigration of the Tagamet®/ethanol solution is not relevant to excuse its non-disclosure.[15]

[15] It is interesting that Glaxo now argues that ranitidine and cimetidine are so different that cimetidine would not be material and yet, during the prosecution of the '249 patent application,

V. CONCLUSION

There is evidence and inferences from the evidence to support Teva's claim that Dr. Hempenstall intentionally withheld stability data from the Patent Office and that this withheld evidence would have prevented him from arguing that the data showed a "highly significant" improvement.

There is evidence and inferences from the evidence to suggest that Dr. Long intentionally did not disclose the closest piece of prior art, the Tagamet®/ethanol solution, which had more features of the invention than any other single piece of prior art cited in the prosecution history. Dr. Long knew of the Tagamet®/ethanol solution, and yet, he did not disclose it.

For the aforementioned reasons, Glaxo's motion to dismiss Teva's inequitable conduct defense and counterclaim should be denied.

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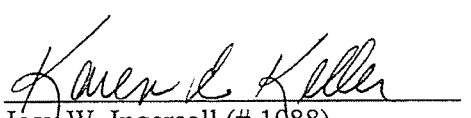

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Glaxo cited the '938 application that referred to both ranitidine and cimetidine in the same application. (G000147, G000150, lines 52-57).

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Dated: July 28, 2006

CERTIFICATE OF SERVICE

I, Karen E. Keller, Esquire, hereby certify that on July 28, 2006, I caused to be electronically filed a true and correct copy of the foregoing document with the Clerk of the Court using CM/ECF, which will send notification that such filing is available for viewing and downloading to the following counsel of record:

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